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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/540,934	HARMON, JOHN W	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *8-13,16,25-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,14,15 and 17-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/23/06,6/29/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 1-40 are pending.

Election/Restrictions

Applicant's election of Group I (claims 1-24) and species cutaneous wound, growth factor HIF-alpha in the reply filed on 6/6/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 25-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and Claims 8-13 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/6/06.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or

provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/437,392 and 60/471,829, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Instant claim 3 does not have written support '1 to 100 pulses' in either '392 or '829. Thus, instant claim 3 only has priority to the PCT filed on 12/29/03.

Instant claim 5 does not have written support '10 to 5,000 V/cm' in either '392 or '829. Thus, instant claim 5 only has priority to the PCT filed on 12/29/03.

Instant claim 14 is does not have written support in application '392 for 'HIF-1alpha'. Thus, instant claim 14 only has priority to '829 filed on 5/20/03.

Instant claim 18 does not have written support 'one or more nucleic acids encoding at least two growth factors' in either '392 or '829. Thus, instant claim 18 only has priority to the PCT filed on 12/29/03.

Instant claim 22 and claims dependent therefrom does not have written support for the limitation 'applying between 1 and 20 pulses of between 500 and 2,000 V/cm and between 10 to 1000 microseconds' in either '392 or '829. Thus, instant claim 22 and claims dependent therefrom only has priority to the PCT filed on 12/29/03.

Information Disclosure Statement

The examiner has considered the international search report.

Specification

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Claim Objections

Claim 24 is objected to because of the following informalities: the period is missing at the end of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 14, 15, and 17-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for applying an electric field to the wound site in an amount to increase transfection of the nucleic acid and administering a nucleic acid encoding a growth factor operably linked to a promoter, does not reasonably provide enablement for applying an electric field to the wound site in an amount sufficient to increase expression of the encoded growth factor and a nucleic acid not operably linked to a promoter. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims encompass applying an electric field to wound site in an amount sufficient to increase expression of the encoded growth factor.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (United States v. Technologies Inc., 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather a conclusion reached by many factors. These factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in In Re Wands (see above).

Furthermore, with respect to claimed method, the claims encompass applying an electric field to the wound site in an amount sufficient to increase the expression of the encoded growth factor. However, it appears that the teaching in the specification is directed to increasing the transfection rate of the nucleic acid to the wound site using the electric field. The specification provides sufficient guidance for one skilled in the art to use an electric field to enhance transfection of DNA into the wound site of the patient. However, the instant specification fails to provide sufficient guidance or factual evidence for one skilled in the art to use an electric field to increase expression of the encoded growth factor in the wound site. To increase expression in the wound site, the encoded growth factor would have to respond to the electric field or contain a regulatory region that would respond to electric field. The guidance or factual evidence in the specification is nil with respect to using an electric field to increase expression of the encoded growth factor in the wound site. The instant specification provides guidance or evidence for how

to apply an electric field to the wound site to increase transfection of DNA to the wound site, however the claims do not recite such a limitation. Thus, to the extent the claims fail to recite distinguishing features to commensurate with the level of guidance presented, the claims are not considered fully enabled.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made do not provide enablement for practicing the full scope of the claimed invention. Given that increasing expression of the encoded growth factor in response to an electric field was unpredictable at the time the invention was made, and given the lack of sufficient guidance for using an electric field, one skilled in the art would have to engage in a large quantity of undue experimentation in order to practice the claimed invention based on the applicant's disclosure.

In addition, with respect to claims 1-7, 14, 15, and 17-24, the claims encompass a nucleic acid comprising a promoter not operatively to a specific nucleotide sequence (e.g. nucleotide sequence encoding a growth factor). The specification provides sufficient guidance for one skilled in the art to make and use a recombinant vector (plasmid), which expresses a growth factor protein comprising (a) promoter operatively linked to a nucleic acid encoding a growth factor. However, the instant specification fails to provide sufficient guidance or evidence for one skilled in the art to make and use a recombinant vector, which express growth factor comprising a promoter that is not operatively linked to any specific nucleotide sequence (e.g. nucleotide sequence encoding a growth factor) in the vector. The teachings in the specification are directed to using a promoter to express the nucleic acid. The specification provides sufficient guidance or factual evidence for how to make and use vectors comprising a promoter operatively linked to a

nucleic acid to direct growth factor expression, however the claims do not recite such a structural limitation. Thus, to the extent the claims fail to recite distinguishing features to commensurate with the level of guidance presented, the claims are not considered enabled.

In conclusion, the instant specification and claims coupled with the state of the art at the time the invention was made provide enablement for a method to promote wound healing in a patient comprising administering a nucleic acid operatively linked to a promoter and not for the full scope of the claimed invention. However, the rest of the disclosure encompassing a genus of nucleic acids comprising a promoter not operatively linked to a nucleotide sequence from the nucleic acid is not considered enabled for the reasons set forth above. Given that making a nucleic acid which expresses a growth factor comprising a promoter not operatively linked to a nucleotide sequence in the nucleic acid was unpredictable at the time the invention was made, and given the lack of sufficient guidance for producing the claimed nucleic acid, one skilled in the art would have to engage in a large quantity of undue experimentation in order to practice the full scope of the claimed invention based on the applicant's disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

In view of compact prosecution, the claimed methods embrace a method of promoting wound healing in a patient comprising administering a nucleic acid encoding a growth factor to a wound site of the patient and applying an electric field to enhance the delivery of the nucleic acid to the cells of the wound site.

Claims 1, 2, 3, 5, 6, 7, 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. (US 6,972,013). Zhang teaches delivery of naked DNA to skin by non-invasive in vivo electroporation (columns 1, 7, and 39-45). Zhang teaches that, "some electroporation applications, the electric field comprises a single wave pulse on the order of 100 to 500 V/cm, of about 10 to 60 ms, duration" (column 3). "Such a pulse may be generated, for

example, in known applications of the Electro Square Porator T820 or ECM830, made by the BTX Division of Genetronics, Inc." See column 3. In the instant specification, the Applicant uses ECM830 for square wave pulse. Zhang teaches, "Although various terms are frequently used herein in the singular, the singular forms of the terms include multiple pulses". See column 7. Zhang teaches that a nucleic acid encoding a growth factor can be used in the method (column 11). A plasmid can be used in the method (column 12). Zhang teaches using a square wave pulse wherein the pulse is at least 50 V for about 10 up to 20 ms (column 15 and 21). The pulse length can be adjusted from 5 μsec to 99 ms (column 21). DNA expression in the epidermis can be used in the acceleration of wound healing (column 45).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, namely to administer to a wound site in a patient a nucleic acid encoding growth factor operably linked to a promoter to the skin via electroporation. One of ordinary skill in the art would have been motivated to practice the claimed method because electroporation to the skin is non-invasive route of gene delivery and the electrodes are user-friendly electrodes. In addition, one of ordinary skill in the art would have been motivated to administer a nucleic acid encoding a growth factor to a wound site because growth factors are known to one of ordinary skill in the art for treating wounds.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, namely to apply the electric field in pulses. One of ordinary skill in the art would have been motivated to practice the claimed method because Zhang teaches that number of pulses appeared to have little influence on the level of stimulation of gene expression

(column 45). See Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, namely to use an electric field from 10 to 5,000 V/cm. One of ordinary skill in the art would have been motivated to practice the claimed method because electric field for in vivo electroporation are preferably from about 700 V/cm to 1300 V/cm as exemplified by Zhang (column 21). See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, namely to use a square wave pulse. One of ordinary skill in the art would have been motivated to practice the claimed method because the square wave pulse is a preferred pulse for delivering a nucleic acid in vivo as exemplified by Zhang (columns 15 and 21). See Sinclair & Carroll Co. v. Interchemical Corp.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, namely to administer to a wound site in a patient a plasmid comprising a nucleic acid encoding growth factor operably linked to a promoter to the skin via electroporation. One of ordinary skill in the art would have been motivated to practice the claimed method because plasmids are suitable vector for use in electroporation of DNA to skin cells as exemplified by Zhang (Column 39). See Sinclair & Carroll Co. v. Interchemical Corp.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made, namely to surgically removed the wound eschar before administering to a wound site in a patient a plasmid comprising a nucleic acid encoding growth factor operably linked to a promoter to the skin via electroporation. One of ordinary skill in the art would have

been motivated to practice the claimed method because to avoid delivering the nucleic acid to the dead skin tissue.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1-7, 15, and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bureau et al. (WO 99/01157, English equivalent is US 6,528,315) taken with Ruben et al. (US 20030186904). Since the WO document is in French, the teaching of US 6,528,315 will be cited in the rejection.

Bureau teaches using electroporation to deliver a transgene to cells of the tissues being treated for either correction of dysfunction of the cells themselves or regeneration of vasulcarization by angiogenic factors produced by the transgene (column 4). In addition, genes encoding growth factors can be delivered (column 6). The cells are brought into contact with the transgene by topical administration (column 3). "The intensity of the field if between 200 V/cm and 600 V/cm and the total duration is greater than 10 milliseconds" (Column 3). "The number of pulses used is from 1 to 1,000 pulses" (column 3). The electrical pulses can be square wave pulses (column 3). A plasmid can be used to deliver the gene (column 24). However, Bureau does not specifically teach using the method to treat a wound in a patient.

However, at the time the invention was made, Ruben teaches that growth factors can be used in therapeutics in the treatment of wounds, burns and other skin disorders (pages 1, 64-69, 88-89 and 134). Ruben further teaches that the administration of a nucleic acid encoding KGF-2 in conjunction with one or more additional nucleic acids that promotes wound healing (page 67).

Ruben teaches the electroporation can be used in the gene therapy method (page 69). Ruben teaches using KGF-2 polynucleotide to stimulate wound healing in the normal rat and diabetic mice (page 134).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to administer a nucleic acid encoding a growth operably linked to a promoter to a wound site and applying an electric field to the wound site to increase transfection of the cells in the wound site. One of ordinary skill in the art would have been motivated to combine the teaching because electroporation is a non-invasiveness method of gene therapy and enhances the method of gene therapy.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to use the electric field in pulses. One of ordinary skill in the art would have been motivated to combine the teaching because pulses are known to one of ordinary skill in the for delivering nucleic acids to cells in vivo as exemplified by Bureau (column 3). See Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to wherein the pulse is from 1 microsecond to 5 seconds in duration. One of ordinary skill in the art would have been motivated to combine the teaching because the duration of the pulse was well known to one or ordinary skill in the art as exemplified by Bureau (column 3). See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to use an intensity between 200 V/cm and 600 V/cm as the electric field. One of ordinary skill in the art would have been motivated to combine the teaching because the intensity between 200 V/cm and 600 V/cm is known to one of ordinary skill in the for delivering nucleic acids to cells in vivo as exemplified by Bureau (column 3). See Sinclair & Carroll Co. v. Interchemical Corp.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to use a square wave pulse as the pulse. One of ordinary skill in the art would have been motivated to combine the teaching because square wave pulse is known to one of ordinary skill in the for delivering nucleic acids to cells in vivo as exemplified by Bureau (column 3). See Sinclair & Carroll Co. v. Interchemical Corp.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to treat a cutaneous wound. One of ordinary skill in the art would have been motivated to combine the teaching to promote wound healing.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to treat a burn. One of ordinary skill in the art would have been motivated to combine the teaching to promote wound healing.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely

to treat a wound in a diabetic patient. One of ordinary skill in the art would have been motivated to combine the teaching to promote wound healing in the diabetic patient.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to surgically removed the wound eschar before administering to a wound site in a patient a plasmid comprising a nucleic acid encoding growth factor operably linked to a promoter to the skin via electroporation. One of ordinary skill in the art would have been motivated to practice the claimed method because to avoid delivering the nucleic acid to the dead skin tissue.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to treat a decubitus ulcer. One of ordinary skill in the art would have been motivated to combine the teaching to promote wound healing in a patient with bed sores.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to use one or more nucleic acids encoding at least two growth factors. One of ordinary skill in the art would have been motivated to combine the teaching to enhance the promotion of wound healing.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau taken with Ruben, namely to use a plasmid as the nucleic acid. One of ordinary skill in the art would have been motivated to combine the teaching because one of ordinary skill in the art uses plasmids for in vivo gene transfer. See Sinclair & Carroll Co. v. Interchemical Corp.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 14, 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bureau et al. (WO 99/01157, English equivalent is US 6,528,315) taken with Ruben et al. (US 20030186904) as applied to claims 1-3, 5-7, 15, and 17-20 above, and further in view of Arbeit (US 6,838,430).

Bureau taken with Ruben do not specifically teach using a nucleic acid encoding HIF-1 alpha.

However, at the time the invention was made, Arbeit teaches using a nucleic acid encoding HIF-1alpha to accelerate wound healing in a patient (columns 2-3 and 8).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau and Ruben in further view of Arbeit, namely to use a nucleic acid encoding HIF-1alpha in the method. One of ordinary skill in the art would have been motivated to combine the teaching to accelerate wound healing in a patient with a wound.

Furthermore, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau and Ruben in further view of Arbeit, namely to apply between 1 to 20 pulses of between 500 and 2000 V/cm and between 10 and 1000 microseconds to the wound site. One of ordinary skill in the art would have been motivated to combine the teaching because Bureau teaches that those limitations read on standard conditions for one of ordinary skill in the art uses when delivering a nucleic acid in

vivo using electroporation. See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau and Ruben in further view of Arbeit, namely to surgically removed the wound eschar before administering to a wound site in a patient a plasmid comprising a nucleic acid encoding growth factor operably linked to a promoter to the skin via electroporation. One of ordinary skill in the art would have been motivated to practice the claimed method because to avoid delivering the nucleic acid to the dead skin tissue.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Bureau and Ruben in further view of Arbeit, namely to use a plasmid as the nucleic acid. One of ordinary skill in the art would have been motivated to combine the teaching because one of ordinary skill in the art uses plasmids for in vivo gene transfer. See Sinclair & Carroll Co. v. Interchemical Corp.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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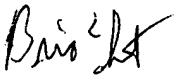
Brian Whiteman



BRIAN WHITEMAN
PATENT EXAMINER